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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

CLOW, LORI A

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 08/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/928,191	Applicant(s) SCHILLING, CHRISTOPHE	
	Examiner Lori A. Clow, Ph.D.	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 10-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I (claims 1-15) and the species encompassing the combination of organism and metabolite of a disease producing, pathogenic organism and a metabolite necessary for its survival in the reply filed on 17 November 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-9 read on the elected species and will hereby be examined.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Although one could argue that the method of analyzing the production of one or more selected metabolites of a biochemical reaction network is useful in further research to identify potentially useful compounds that may be elucidated by identification of deleting pathways to determine essential pathway components, there is no specificity identified as to what types of compounds are being generated or what the immediate result of the method is. Therefore, the invention does not meet the standard of being immediately useful. The need to do extensive work does not meet the "concrete, tangible, and useful" result standard set forth in MPEP 2106.

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MPEP 2106: “For such subject matter to be statutory, the claimed process must be limited to a practical application of the abstract idea or mathematical algorithm in the technological arts. See *Alappat*, 33 F.3d at 1543, 31 USPQ2d at 1556-57 (quoting *Diamond v. Diehr*, 450 U.S. at 192, 209 USPQ at 10). See also *Alappat* 33 F.3d at 1569, 31 USPQ2d at 1578-79 (Newman, J., concurring) (“unpatentability of the principle does not defeat patentability of its practical applications”) (citing *O’Reilly v. Morse*, 56 U.S. (15 How.) at 114-19). A claim is limited to a practical application when the method, as claimed, produces a concrete, tangible, and useful result; i.e., the method recites a step or act of producing something that is concrete, tangible, and useful. See *AT&T*, 172 F.3d at 1358, 50 USPQ2d at 1452. Likewise, a machine claim is statutory when the machine, as claimed, produces a concrete, tangible, and useful result (as in *State Street*, 149 F.3d at 1373, 47 USPQ2d at 1601) and /or when a specific machine is being claimed (as in *Alappat*, 33 F.3d at 1544, 31 USPQ2d at 1557 (in banc)).”

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 1 recites “in consideration of the exchange fluxes”. It is unclear what is meant by this phrase. Does Applicant intend that the stoichiometric matrix contains representations of the exchange fluxes? It is unclear from where the exchange fluxes are derived. Clarification is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 9 is drawn to a drug developed in accordance with the method of claim 8. However, the specification fails to describe any drug “developed” by the method of claim 8. Claim 8 recites using the reaction set to “target development” of a drug, but the specification fails to described any steps of developing or synthesizing a drug, not any particular drugs or compounds “targeted” by a particular set of reactions. As such, claim 9 lacks written description.

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9 are rejected under 35 U.S.C. 102(a) as being anticipated by Schilling et al.

(Biotechnol. Bioeng. (2000/2001) Vol. 71, pages 286-306; published online 30 March 2001).

The instant invention is drawn to a method of analyzing the production of one or more selected metabolites of a biochemical reaction network producing metabolites wherein the method has as inputs biochemical reactions, exchange fluxes, a stoichiometric matrix developed from the reactions, and a system of equations.

Schilling et al. teach a method for combining pathway analysis with flux balance analysis for the comprehensive study of metabolic systems. In particular, Schilling et al. teach a method to study the systemic properties of cellular metabolism. With regard to claim 1, Schilling et al. teach biochemical reactions of a metabolic system in which pathways are defined by a flux space within the context of convex analysis (abstract). The flux space of the system is constrained in a convex polyhedral cone in high-dimensional space. The edges of the flux cone are vectors that correspond to “extreme pathways” spanning the capabilities of the system (abstract). The flux balance analysis is done using linear optimization to calculate the flux distributions. The metabolic shifts of behavior are analyzed such that changes to the reaction network, such as removal of a reaction, can lead to the generation of suboptimal phenotypes that can be directly attributable to the loss of pathway function and capabilities (abstract).

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In regard to claim 2, Schilling et al. teach that if a reaction is eliminated or constrained to zero, all of the pathways that utilize the reaction will be eliminated. The changes in pathway utilization allow for interpretation of metabolic shifts in terms of underlying pathways of a network (page 292, column 2).

In regard to claim 3, the mathematical process is convex analysis (abstract and page 289, column 1).

In regard to claim 4, convex analysis comprises calculating linear equations and inequalities (page 289, column 1).

In regard to claim 5, reactions have associated constraints placed upon the direction in which the reaction can proceed (page 929, column 1).

In regard to claims 6 and 7, the output consists of functional properties of interest which can be diminished or eliminated (page 292, column 2).

In regard to claim 8, Schilling et al. teach a reaction network which represents a disease producing, pathogenic organism (E. coli) and the metabolite of interest that is necessary for its survival is glucose or succinate (pages 294-295; see Pathway Analysis for the Linked Output System, especially).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schilling et al. ((Biotechnol. Bioeng. (2000/2001) Vol. 71, pages 286-306; published online 30 March 2001), for the reasons set forth above as the rejections pertain to claims 1-8.

Schilling et al. do not specifically teach the limitations of claim 9 (a drug developed in accordance with the method of claim 8), however, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have developed a drug using the methods of Schilling et al. for pathway analysis with flux balance in order to develop a drug that would obstruct a reaction or reactions necessary for survival of a pathogen. Schilling et al. motivate one to do so by stating that "flux balance and pathway analysis for studying metabolic

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systems along with the combination of emerging genome-scale experimental technologies should serve to form a useful platform from which to study the complexity inherent in cellular metabolism from both the scientific and applied purpose of **metabolic engineering** and biocommodity engineering (pages 287-288)".

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

August 8, 2005
Lori A. Clow, Ph.D.
Art Unit 1631
Lori A. Clow

MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran
8/8/05